

Applicants : Hilton A. Salhanick and Joachim Hourihan  
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matter thereof in a future application.

Please add new claims 94-129 as follows:

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94. (New) A method of diagnosing a thyroid condition in a subject which comprises:

- B1
- a) obtaining a <sup>102, 2.2</sup> suitable urine sample from the subject;
  - b) determining the concentration of thyroid stimulating hormone in the sample by a method which is not a <sup>9.9</sup> radioimmunoassay; and
  - c) comparing the concentration of thyroid stimulating hormone with a urinary concentration of thyroid stimulating hormone in a normal subject;

wherein:

- i) a concentration of thyroid stimulating hormone which is higher than the urinary concentration of thyroid stimulating hormone in the normal subject diagnoses hypothyroidism in the subject; and
- ii) a concentration of thyroid stimulating hormone which is lower than the urinary concentration of thyroid stimulating hormone in the normal subject diagnoses hyperthyroidism in the subject.

95. (New) The method of claim/94, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroid stimulating hormone with the urine sample so as to bind thyroid stimulating hormone which is present in the sample to the agent;

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- (2) removing unbound urine sample;
- (3) contacting the bound thyroid stimulating hormone with a detectable agent capable of binding to thyroid stimulating hormone so as to bind the detectable agent to the bound thyroid stimulating hormone;
- (4) removing unbound detectable agent; and
- (5) determining the amount of detectable agent which is bound to the thyroid stimulating hormone, thereby determining the amount of thyroid stimulating hormone in the urine sample.
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96. (New) The method of claim 95, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is an antibody which binds to thyroid stimulating hormone.
97. (New) The method of claim 95, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is a thyroid stimulating hormone receptor.
98. (New) The method of claim 95, wherein the detectable agent is an antibody which binds to an epitope on thyroid stimulating hormone which differs from the epitope to which the agent of step (1) binds.
99. (New) The method of claim 95, wherein the detectable agent is labeled with a detectable marker.
100. (New) The method of claim 94, wherein a concentration greater than 0.35  $\mu$ IU/ml diagnoses hypothyroidism in the subject.

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101. (New) The method of claim 94, wherein a concentration less than 0.04  $\mu$ IU/ml diagnoses hyperthyroidism in the subject.

102. (New) A method of diagnosing a thyroid condition in a subject which comprises:

- a) obtaining a suitable urine sample from the subject;
- b) determining the concentration of thyroxine present in the sample by a method which is not a radioimmunoassay; and
- c) comparing the concentration of thyroxine with a urinary concentration of thyroxine in a normal subject;

wherein

- i) a concentration of thyroxine which is lower than the concentration of thyroxine in the normal subject diagnoses hypothyroidism in the subject; and
- ii) a concentration of thyroxine which is higher than the urinary concentration of thyroxine in the normal subject diagnoses hyperthyroidism in the subject.

103. (New) The method of claim 102, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the

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thyroxine present in the urine sample; and

- (2) determining the amount of detectable thyroxine which is bound to the agent, wherein the difference between the pre-determined amount of detectable thyroxine and the amount of detectable thyroxine which is bound indicates the amount of thyroxine present in the urine sample.

104. (New) The method of claim 102, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample; and
- (2) determining the amount of detectable thyroxine which is not bound to the agent, thereby determining the amount of thyroxine present in the urine sample.

105. (New) The method of claim 103 or 104, wherein the agent of step (1) which is capable of binding to thyroxine is an antibody.

106. (New) The method of claim 103 or 104, wherein the agent of step (1) which is capable of binding to thyroxine is a thyroxine receptor.

107. (New) The method of claim 103 or 104, wherein the detectable thyroxine is labeled with a detectable marker.

108. (New) The method of claim 102, wherein a concentration lower than 0.3 ng/ml diagnoses hypothyroidism in the subject.

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109. (New) The method of claim 102, wherein a concentration higher than 1.5 ng/ml diagnoses hyperthyroidism in the subject.

110. (New) A method of diagnosing a thyroid condition in a subject which comprises:

- a) obtaining a suitable urine sample from the subject;
- b) determining the concentration of thyroid stimulating hormone (and) the concentration of thyroxine in the sample by a method which is not a radioimmunoassay; and
- c) comparing the concentration of thyroid stimulating hormone with a urinary concentration of thyroid stimulating hormone in a normal subject and comparing the concentration of thyroxine with a urinary concentration of thyroxine in a normal subject;

wherein

- i) a concentration of thyroid stimulating hormone which is higher than the urinary concentration of thyroid stimulating hormone in a normal subject, and a concentration of thyroxine which is lower than the urinary concentration of thyroxine in a normal subject, diagnoses hypothyroidism in the subject; and
- ii) a concentration of thyroid stimulating hormone which is lower than the urinary concentration of thyroid stimulating hormone in a normal subject, and a concentration of thyroxine which is higher than the urinary concentration of thyroxine in a

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normal subject, diagnoses hyperthyroidism in the subject.

111. (New) The method of claim 110, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroid stimulating hormone with the urine sample so as to bind thyroid stimulating hormone which is present in the sample to the agent;
- (2) removing unbound urine sample;
- (3) contacting the bound thyroid stimulating hormone with a detectable agent capable of binding to thyroid stimulating hormone so as to bind the detectable agent to the bound thyroid stimulating hormone;
- (4) removing unbound detectable agent; and
- (5) determining the amount of detectable agent which is bound to the thyroid stimulating hormone, thereby determining the amount of thyroid stimulating hormone in the urine sample.

112. (New) The method of claim 111, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is an antibody which binds to thyroid stimulating hormone.

113. (New) The method of claim 111, wherein the detectable agent is an antibody which binds to an epitope on thyroid stimulating hormone which differs from the epitope to which the agent of step (1) binds.

114. (New) The method of claim 111, wherein the agent capable of binding to thyroid stimulating hormone of step (1) is a

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receptor which binds to thyroid stimulating hormone.

115. (New) The method of claim 111, wherein the detectable agent is labeled with a detectable marker.

116. (New) The method of claim 110, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample; and
- (2) determining the amount of detectable thyroxine which is bound to the agent, wherein the difference between the pre-determined amount of detectable thyroxine and the amount of detectable thyroxine which is bound indicates the amount of thyroxine present in the urine sample.

117. (New) The method of claim 110, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample; and
- (2) determining the amount of detectable thyroxine which is not bound to the agent, thereby determining the amount of thyroxine present in the urine sample.

118. (New) The method of claim 116 or 117, wherein the agent of step (1) which is capable of binding to thyroxine is an antibody.

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119. (New) The method of claim 116 or 117, wherein the agent of step (1) which is capable of binding to thyroxine is a thyroxine receptor.
120. (New) The method of claim 116 or 117, wherein the detectable thyroxine is labeled with a detectable marker.
121. (New) The method of claim 110, wherein a concentration of thyroid stimulating hormone greater than 0.35  $\mu$ IU/ml and a concentration of thyroxine greater than 1.5 ng/ml diagnoses hypothyroidism in the subject.
122. (New) The method of claim 110, wherein a concentration of thyroid stimulating hormone less than 0.04  $\mu$ IU/ml and a concentration of thyroxine less than 0.3 ng/ml diagnoses hyperthyroidism in the subject.
123. (New) A method of determining whether a subject being treated with thyroxine is receiving a proper dosage of thyroxine which comprises:
- a) obtaining a suitable urine sample from the subject;
  - b) determining the concentration of thyroxine in the sample by a method which is not a radioimmunoassay; and
  - c) comparing the concentration of thyroxine with a urinary concentration of thyroxine in a normal subject;

wherein a concentration of thyroxine which is higher or lower than the urinary concentration of thyroxine in a normal subject indicates that the subject is not receiving



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the proper dosage of thyroxine.

124. (New) The method of claim 123, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample; and
- (2) determining the amount of detectable thyroxine which is bound to the agent, wherein the difference between the pre-determined amount of detectable thyroxine and the amount of detectable thyroxine which is bound indicates the amount of thyroxine present in the urine sample.

125. (New) The method of claim 123, wherein step (b) comprises:

- (1) contacting an agent capable of binding to thyroxine with a pre-determined amount of detectable thyroxine and the urine sample, so as to form a complex between the agent and (i) the detectable thyroxine or (ii) the thyroxine present in the urine sample; and
- (2) determining the amount of detectable thyroxine which is not bound to the agent, thereby determining the amount of thyroxine present in the urine sample.

126. (New) The method of claim 124 or 125, wherein the agent of step (1) which is capable of binding to thyroxine is an antibody.

127. (New) The method of claim 124 or 125, wherein the agent of step (1) which is capable of binding to thyroxine is a